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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/657,516 | 09/08/2003 | Francois Binette | 022956-0225 | 7793 |

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| EXAMINER | |
|---|---|
| QIAN, CELINE X | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1636 | |

| NOTIFICATION DATE | DELIVERY MODE |
|---|---|
| 03/18/2008 | ELECTRONIC |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docket@nutter.com

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/657,516 | BINETTE ET AL. | |
| | Examiner | Art Unit | |
| | CELINE X. QIAN | 1636 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *03 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *25-59* is/are pending in the application.

4a) Of the above claim(s) *25-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *48-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Claims 25-59 are pending in the application. Claims 25-47 are withdrawn from consideration for being directed to non-elected subject matter. Claims 48-59 are currently under examination.

This office action is in response to the amendment filed on 12/3/07.

### *Response to Amendment*

The rejection of claims 48-51 and 54-56 under 35 U.S.C. 102 (b) is maintained for reason set forth of the record mailed on 10/10/07 and further discussed below.

The rejection of claims 52, 53, 57-59 under 35 U.S.C 103(a) is maintained for reason set forth of the record mailed on 10/10/07 and further discussed below.

### *Response to Arguments*

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 48-51 and 54-56 are rejected under 35 U.S.C. 102(b) as being anticipated by Glorioso et al.

In response to this rejection, Applicants argue that the '511 reference does not teach each and every element of amended claim 48 and thus does not anticipate the claimed invention. Applicants assert that the '511 reference teaches a method for genetically alleviating pathologies of the joint, not to an ectopic site and do not perform the function of cartilage tissue and are not

used for tissue repair or construction. Applicants assert that Glorioso is using the modified chondrocyte-gel composition to treat pathology in a tissue native to chrodroncytes, and cells delivered to treat or repair native tissue will have a high propensity of being incorporated within the tissue at the repair site, which is at odds to the claimed invention. Applicants further assert that Glorioso does not teach using the modified chondrocytes as suitable drug delivery agents for delivering therapeutics to environment that are foreign to those cells, i.e. tissue other than joints. Applicants allege that it is with hindsight that the examiner is able to realize the potential benefits of using modified chondrocytes to treat abnormalities at ectopic sites without the cells performing the function of cartilage tissue or being used for tissue construction. Applicants thus conclude that the claimed invention is not anticipated by Glorioso et al.

The above arguments have been fully considered but deemed unpersuasive. The detailed reason for this rejection was set forth of the record mailed on 10/1/07. In response to the above arguments, Applicants are reminded that the claimed invention is directed to a product, the modified chondrocyte, rather than a process, such as a method of using the chondrocyte as a delivery vehicle to a site that is foreign to chondrocytes. As stated before, the intended use of chondrocyte would only be considered a limitation that distinguish from the prior art if it makes a difference to the structure of the claimed chondrocyte. However, in the instant case, the limitation of "wherein the target region is an ectopic site...and is not used for tissue repair or construction" does not impart a structural difference of the claimed chondrocytes to the chondrocytes disclosed by Glorioso. In other words, if the prior art structure of the chondrocytes is capable of performing the intended use, it meets the limitation. Therefore, for reasons set forth in the previous office action and above, this rejection is maintained.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 52-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glorioso et al., in view of Bartholomew et al.

In response to this rejection, Applicants assert that the '511 reference teaches a method for genetically alleviating pathologies of the joint, not to an ectopic site and do not perform the function of cartilage tissue and are not used for tissue repair or construction. Applicants assert that Glorioso is using the modified chondrocyte-gel composition to treat pathology in a tissue native to chrodroncytes, and cells delivered to treat or repair native tissue will have a high propensity of being incorporated within the tissue at the repair site, which is at odds to the claimed invention. Applicants further assert that Glorioso does not teach using the modified chondrocytes as suitable drug delivery agents for delivering therapeutics to environment that are foreign to those cells, i.e. tissue other than joints. Applicants argue that Bartholomew does not teach or suggest using a biocompatible substrate in place of the IID's to deliver genetically modified cells or EPO mimetibody. Applicants further argue that Bartholomew fail to disclose the use of genetically altered chondrocytes for expressing EPO or its mimetibody, or the ability of the modified chondrocytes to express the therapeutic when delivered at an ectopic site. Applicants further assert that Bartholomew does not teach the elements of claim 48, 52 and 53, and fail to remedy the deficiency of Glorioso et al. Applicants also argue that it is examiner's

burden to show why one of ordinary skill in the art would consider substituting the mesenchymal stem cells disclosed in Bartholomew with chondrocytes expressing EPO or its minetibody, and replace the immunosiolatory devices with a biocompatible matrix. Applicants thus conclude that the claimed invention is not obvious in view of the combined teaching of Glorioso and Bartholomew.

The above arguments have been fully considered but deemed unpersuasive. The detailed reason for this rejection was set forth in previous office action. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). It would have been obvious to one of ordinary skill in the art to express erythropoietin or erythropoietin mimetibody in the chondrocyte taught by Glorioso et al. and combined with a biocompatible substrate based on the general knowledge in the art at the time of filing. The claimed invention would have been obvious because the substitution of one known element for another would have yielded predictable results to one of ordinary skill in the art. As evidenced by the teaching of Glorioso et al., one of ordinary skill in the art would have reasonable expectation of success in introducing a transgene into chondrocyte and express said protein *in vitro* or *in vivo,* and following the guidance of Bartholomew, one of ordinary skill in the art would have reasonable expectation of success in introducing the coding sequence of human EPO or mimetibody into a vector and express it *in vitro* or *in vivo.* Therefore, the invention would have been *prima facie* obvious to an ordinary artisan at the time the invention was made. At the time of filing, there are many ways of delivering cells to a given site in an

animal as evidenced by Bartholomew and Glorioso such as using IID or using biocompatible substrate. It is not the novelty of the claimed invention of using any device to deliver the genetically modified chondrocytes. Glorioso et al. discloses that chondrocytes may express a polypeptide of interest including interleukins, cytokines, tumor necrosis factors and biologically fragment thereof. EPO is a cytokine for erythrocyte precursors in bone marrow. While the nucleic acid sequence that expresses EPO is known at the time of filing, substituting the transgene transfected to the chondrocyte as disclosed by Glorioso with construct expressing EPO or fragment thereof would have yield predictable results to one of ordinary skill in the art, wherein the result is expressing EPO in said chondrocyte. KSR forecloses the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness. As such, based on the combined teaching of Glorioso and Bartholomew, an ordinary skilled in the art would realize that all the claimed elements were known in the prior art at the time of filing, and would have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to the ordinary artisan at the time of filing. Absent evidence from the contrary, the claimed invention would have been *prima facie* obvious in view of the teaching of Glorioso and Bartholomew at the time of filing.

Claims 57-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glorioso et al., in view of Okada et al.

In response to this rejection, Applicants argue that the claimed invention is not obvious for same reason as discussed above because Okada et al. do not teach all the elements in claim 48 and does not remedy the deficiency of Glorioso et al.

The above arguments have been considered but deemed unpersuasive for same reason as discussed above. Therefore, this rejection is maintained.

***Conclusion***

No claims are allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CELINE X. QIAN whose telephone number is (571)272-0777. The examiner can normally be reached on 10-6:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joe Woitach Ph.D. can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Celine X Qian Ph.D./
Primary Examiner, Art Unit 1636